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FACULDADE DE MEDICINA DENTÁRIA

THE CHEMICAL INTERACTION BETWEEN ENDODONTIC IRRIGANTS: A LITERATURE REVIEW

MOHAMMED ALMUFDI

DISSERTAÇÃO

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Dissertação orientada pelo

Prof. Doutor. : António Ginjeira

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To my country and its beautiful revolution,
To myself

Resumo

Introdução:

O objetivo do tratamento endodôntico é a remoção de todos os tecidos vitais ou necróticos, microrganismos e subprodutos dos microbianos do sistema dos canais radiculares. Isto pode ser alcançado através do desbridamento químico-mecânico do canal radicular. O sistema de canais radiculares é altamente complexo e variável e limita a nossa capacidade de os limpar e desinfetar de maneira previsível. A modelagem dos canais radiculares é realizada quase inteiramente usando técnicas manuais e de instrumentação rotativa. Utilizando micro tomografia computadorizada, antes e após a instrumentação mecânica, constatou-se que, independentemente da técnica de instrumentação, os canais preparados ficaram significativamente mais arredondados, com maiores diâmetros e mais rectos que os canais não preparados. No entanto, 35% ou mais das superfícies do canal radicular (incluindo canal fins, istmo e fundos de saco) permaneceram sem instrumentação (Ganahl, Peters, & Paqué, 2009). Portanto, a irrigação é uma parte essencial do desbridamento do canal radicular porque permite a limpeza além da que pode ser alcançado apenas pela instrumentação do canal radicular.

No entanto, não há atualmente nenhum irrigante exclusivo que atenda a todos os requisitos para uma solução ótima de irrigação (Kandaswamy & Venkateshbabu, 2010). Para isso, a combinação de dois ou mais irrigantes para atender a maioria dos requisitos de um irrigante ideal é uma prática antiga e amplamente realizada por dentistas. A importância disso é que, mesmo quando as soluções não são misturadas diretamente, elas entrarão em contato umas com as outras e poderão interagir quimicamente, formando subprodutos indesejados, que podem ser tóxicos, irritantes, com propriedades físicas indesejáveis, como descoloração das cores ou efeito enfraquecedor da capacidade adesiva à parede dentinária (Nascimento Santos et al., 2006); (Wright, Kahler e Walsh, 2017). A mistura ou irrigação alternada também pode alterar sua capacidade de limpar e desinfetar o sistema dos canais radiculares, alterando sua estrutura química com a subsequente perda do agente ativo (Kuruvilla & Kamath, 1998), ou induzindo a formação de precipitado no sistema de canais radiculares. Precipitados podem ocluir os túbulos dentários, resultando em menor penetração de antimicrobianos e perda da eficácia da desinfeção (Wright, Kahler, & Walsh, 2017). O uso de uma combinação de produtos na sequência correta de irrigação e técnica poderia contribuir para o sucesso do tratamento.

Objetivo:

O objetivo deste trabalho é avaliar a eficácia da combinação dos irrigantes mais utilizados no tratamento endodôntico e caracterizar os subprodutos formados nas associações entre eles, a citotoxicidade e os efeitos bacteriostáticos ou bactericidas das combinações, as várias cores destes subprodutos e seus efeitos na restauração final, taxa de sucesso e micro-infiltração em cada tipo de reação. Assim, o resultado final será descobrir a melhor sequência de irrigação possível e saber que tipos de combinações de irrigantes são aconselháveis e as que devem ser evitadas.

Métodos:

Este estudo foi realizado como uma revisão de literatura na área de irrigantes endodônticos. Para tanto, foi realizada uma pesquisa nas bases de dados *PubMed* e *Scielo*, no período de novembro de 2017 a maio de 2019, com os seguintes critérios de inclusão: artigos em inglês e português e de 1973 até o presente. Relatos de Casos, estudos clínicos, Meta-análises, revisões narrativas e revisões sistemáticas. As palavras-chave utilizadas foram "irrigantes do canal radicular" e "irrigantes endodônticos" com "combinação", "interação" e "comparação". Alguns livros também foram incluídos. A partir da pesquisa inicial, e após a leitura dos resumos, foram selecionados 19 artigos. Durante o desenvolvimento do trabalho, houve a necessidade de ampliar os artigos de pesquisa previamente selecionados, a fim de complementar as informações, por meio de uma bibliografia associada. Assim, foi finalizado com 38 artigos finais. Houve também necessidade de rever as interacções químicas dos irrigantes endodônticos, bem como conceitos de desbridamento químico-mecânico para melhor compreensão desta revisão narrativa.

Conclusões:

A irrigação tem um papel fundamental no sucesso do tratamento endodôntico. O principal objetivo do tratamento do canal radicular é eliminar completamente os diferentes componentes do tecido pulpar, bactérias e biofilme e produzir um selo hermético para prevenir a infecção ou reinfecção e promover a cicatrização dos tecidos circundantes. O tempo extra que ganhamos usando instrumentos rotatórios (sistemas mecanizadas) de NiTi deve ser usado para irrigação abundante a fim de obter uma melhor limpeza do sistema de canais radiculares, contribuindo assim para melhorar o sucesso do tratamento. A solução de irrigação mais utilizada é o hipoclorito de sódio. Embora o hipoclorito de sódio tenha muitas qualidades e propriedades desejáveis, por si só não é suficiente para limpar totalmente o sistema de canais radiculares de detritos e biofilmes orgânicos e inorgânicos.

Para uma irrigação ideal, deve ser usada uma combinação de diferentes soluções de irrigação. O dentista deve estar ciente das interações entre os vários produtos químicos encontrados em irrigantes, pois eles podem enfraquecer a atividade do outro e resultar no desenvolvimento de produtos que são prejudiciais ao hospedeiro. O subproduto mais preocupante é o precipitado castanho-alaranjado (PCA) observado na associação entre CHX e NaOCl devido à sua citotoxicidade, resistência a ser removida, capacidade de oclusão dos canais da dentina, micro-infiltração e falha do tratamento endodôntico. NaOCl e EDTA levaram principalmente à formação de gás cloro (Cl_2), que parecia estar dentro dos limites tolerável. A reacção menos indesejável foi de CHX com EDTA e foi menos prejudicial ao tratamento endodôntico, resultando em precipitado branco que foi associado com reação ácido-base. QMiX é seguro a usar e nenhum PCA foi detectado quando seguido NaOCl como a lavagem final.

A maioria dos estudos sugere que os fluxos intermediários com água destilada parecem ser apropriados para prevenir ou pelo menos reduzir a formação dos subprodutos, com a exceção da formação de PCA da reação (NaOCl-CHX). Que os produtos químicos sejam administrados de forma adequada para libertar todo o seu potencial é imperativo para o sucesso do tratamento endodôntico. Um protocolo de irrigação sugerido por (B. Basrani & Haapasalo, 2012), apresentado no fim do trabalho (Figura 7), é altamente recomendável até que mais estudos sejam feitos.

Abstract

Introduction: The goal of endodontic therapy is the removal of all vital or necrotic tissue, microorganisms, and microbial by-products from the root canal system. This may be achieved through chemomechanical debridement of root canal. In this review article, the specifics of the pulpal microenvironment and the resulting requirements for irrigating solutions are spelled out. Sodium hypochlorite solutions are recommended as the main irrigants. This is because of their broad antimicrobial spectrum as well as their unique capacity to dissolve necrotic tissue remnants. Chemical and toxicological concerns related to their use are discussed, including different approaches to enhance local efficacy without increasing the caustic potential. In addition, chelating solutions are recommended as adjunct irrigants to prevent the formation of a smear layer and/or remove it before filling the root canal system. Along with traditional irrigants, newer irrigants are also studied for potential replacement of sodium hypochlorite. This article reviews the potential irrigants with their advantages and limitations with their future in endodontic irrigation. Based on the actions and interactions of currently available solutions, a clinical irrigating regimen is proposed. Furthermore, some technical aspects of irrigating the root canal system are discussed, and recent trends are critically inspected.

Method: The research was done on the data bases *PubMed* e *Scielo*, from November 2017 until May 2019, with the **key-words**: ‘root canal irrigants’ and ‘endodontic irrigants’ with ‘combination’, ‘interaction’ ‘Evaluation’ and ‘comparison’. The articles included are from 1973 until now, however, it was needed to use articles previous of that date. Books were also used.

Conclusion: After this review it is possible to conclude that the combination of NaOCl and CHX should be avoided, other irrigants combinations’ outcomes are less harmful and could be overcome by using water, saline or ethanol flushes and drying out with paper points.

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Abbreviations and Units:

PCA: P-Chloroaniline (Formula: C_6H_6ClN). Has Other names like: 4-Chloroaniline; Aniline, p-chloro-; p-Aminochlorobenzene; p-Chlorophenylamine; p-Ca; 4-Chlorobenzenamine; Benzenamine, 4-chloro-; p-Chloraniline; among others.

CHX: Chlorhexidine (Formula: $C_{22}H_{30}Cl_2N_{10}$)

EDTA: Ethylenediaminetetraacetic acid. Has other names like: *N*,*N′*-Ethane-1,2-diylbis[*N*-(carboxymethyl)glycine]; Diaminoethane-tetraacetic acid; Edetic acid; Ethylenedinitrilo-tetraacetic acid; Versene

NaOCL: Sodium Hypochlorite (Formula: NaOCl). Has other names like: Antiformin; Bleach; Chloride of soda

SEM: scanning electron microscope.

TOF (SIMS) Time-Of-Flight secondary ion mass spectrometry:
Secondary ion mass spectrometry is the mass spectrometry of ionized particles which are emitted when a surface is bombarded by energetic primary particles, usually ions.

ESI-QTOF-MS :
Electrospray ionization quadrupole time-of-flight mass spectrometry (ESI-QTOF-MS) is a hybrid mass spectrometer that is able to associate a soft ionization technique in atmospheric pressure (electrospray ionization) with the high-resolution tandem mass spectrometry (quadrupole plus time-of-flight). ESI-QTOF-MS has been used as an important fingerprint tool for complex samples because of the high mass resolving power and the mass accuracy of TOF analyzer. Moreover, it makes possible a direct insertion of very little amount of sample, without the need of a pre-separation method, as happens with the chromatography technique.

Units:

cP: Centipoise is a dynamic **viscosity** measurement unit. A centipoise (**cP**) is a non-SI (non-System International) measurement unit of dynamic **viscosity** in the centimeter gram second (CGS) system of units

mS: The SI unit of **conductivity** is S/m and, unless otherwise qualified, it refers to 25 °C. Often encountered in industry is the traditional unit of μS/cm.
10^6 μS/cm = 10^3 **mS**/cm = 1 S/cm.

Introduction

The goal of endodontic therapy is the removal of all vital or necrotic tissue, microorganisms, and microbial by-products from the root canal system. This may be achieved through chemomechanical debridement of root canal. The root canal system is highly complex and variable and has limited our ability to clean and disinfect it predictably. Shaping of root canals is performed almost entirely by using hand and rotary instrumentation techniques. Using micro computed tomography scans before and after mechanical instrumentation found that, regardless of the instrumentation technique, prepared canals were significatively more rounded, had greater diameters and were straighter than unprepared canals. However , 35% or more of the root canal surfaces (including canal fins, isthmus and cul-de-sacs) remained uninstrumented (Ganahl, Peters, & Paqué, 2009) . Therefore, irrigation is an essential part of root canal debridement because it allows for cleaning beyond what might be achieved by root canal instrumentation alone.

Characteristics of an ideal endodontic irrigant (Zehnder, 2006**;** B. Basrani & Haapasalo, 2012**;** Hargreaves & Berman, 2015) **:**

1. Effective germicide and fungicide.

2. Non-irritating to the periapical tissues.

3. Stable in solution.

4. Prolonged antimicrobial effect and a sustained antibacterial effect after use.

5. Active in the presence of blood, serum, and protein derivatives of tissue.

6. Able to completely remove the smear layer.

7. Low surface tension.

8. Able to disinfect the dentin/dentinal tubules.

9. Does not interfere with repair of periapical tissues.

10. Does not stain tooth structure.

11. Inactivation in a culture medium.

12. Does not induce a cell-mediated immune response. Is non antigenic, non-toxic, and non-carcinogenic to tissue cells surrounding the tooth.

13. Has no adverse effects on the physical properties of exposed dentin.

14. Has no adverse effect on the sealing ability of filling materials.

15. Easy to use/apply.

16. Inexpensive.

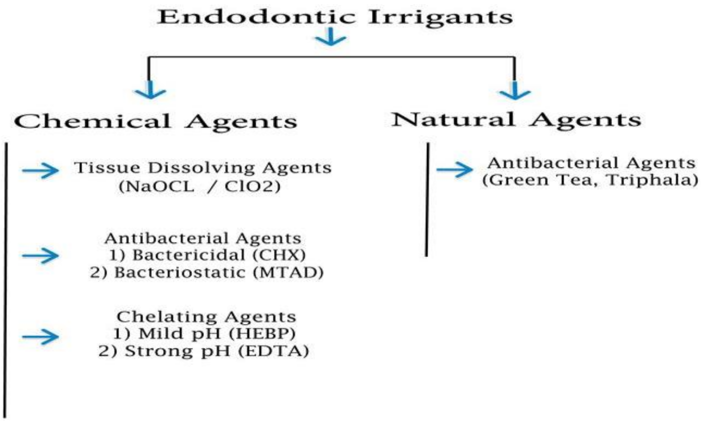


Figure 1: Classification of the commonly used irrigating solutions (Kandaswamy & Venkateshbabu, 2010)

However, there is currently no unique irrigant that meets all of the requirements for an optimal irrigating solution (Kandaswamy & Venkateshbabu, 2010). For that, the combination of two or more irrigants to accomplish most of the requirements of an ideal irrigants is an old and wide practice done by dentists. The importance of this is that because even when solutions are not admixed directly, they will come into contact with one another and may interact chemically, forming unwanted by-products, which may be toxic, irritant, having unwanted physical properties like discoloration or weakening effect of the adhesive ability to dentine wall (Nascimento Santos et al., 2006; Wright, Kahler, & Walsh, 2017). Mixing or alternating irrigants can also alter their ability to clean and disinfect the root canal system of teeth by changing their chemical structure with subsequent loss of the active agent (Kuruvilla & Kamath, 1998), or by inducing precipitate formation in the root canal system. Precipitates may occlude dental tubules, resulting in less penetration of antimicrobials and a loss of disinfection efficacy (Wright, Kahler, & Walsh, 2017). Using a combination of products in the correct irrigation sequence and technique could contribute to a successful treatment outcome.

Objective : The aim of this work is to evaluate the efficacy of the combination of most commonly used irrigants in endodontic practice and characterize the by-products formed in the associations between them, cytotoxicity and bacteriostatic/bactericidal effects of the combinations, the various colors of these by-products and their effects on final restoration, rate of success and the micro-leakage in each type of reaction. Thus, the ultimate result will be to figure out the best irrigation sequence possible and to know which types of irrigants combinations are advisable and which are avoidable.

Methods: This study was carried out as a literature review in the area of Endodontic irrigants. To establish that, a research in the PubMed and Scielo databases from November 2017 to May 2018, with the following inclusion criteria: articles in English and Portuguese and from 1973 to the present. Case Reports, clinical studies, Meta-analyzes, narrative reviews and systematic reviews. The Keywords used were ‘root canal irrigants’ and ‘endodontic irrigants’ with ‘combination’, ‘interaction’ ‘Evaluation’ and ‘comparison’. Some books were also included. From the initial research, and after reading the abstracts, 19 articles were selected. During the development of the work, there was a need to broaden the research articles previously selected in order to complement information, through an associated bibliography. Thus, it was finalized with 38 final articles. There was also a need to review the chemical interactions of the endodontic irrigants as well as concepts of chemo-mechanical debridement for further understanding of this narrative review.

Revision of the reactions of mostly used Endodontic irrigants

A) Sodium hypochlorite: NaOCl is the most commonly used irrigating solution, because of its antibacterial capacity and its ability to dissolve necrotic tissue, vital pulp tissue, and the organic components of dentine and biofilms in a fast manner (Kenneth Hargreaves Louis Berman, 2015) its mode of action described by (Mohammadi, 2008)
that when NaOCl contact tissue proteins, nitrogen, formaldehyde and acetaldehyde are formed. Peptide links are fragmented and proteins disintegrate, permeating hydrogen in the amino groups (-NH-) to be replaced by chlorine (NCl) forming chloramines; this plays an important role for the antimicrobial effectiveness. Necrotic tissue and pus are dissolved and the antimicrobial agent can better reach and clean the infected areas. Sodium hypochlorite exhibits a dynamic balance as shown by the following reaction in (Figure 2), it has a mode of action as follow:

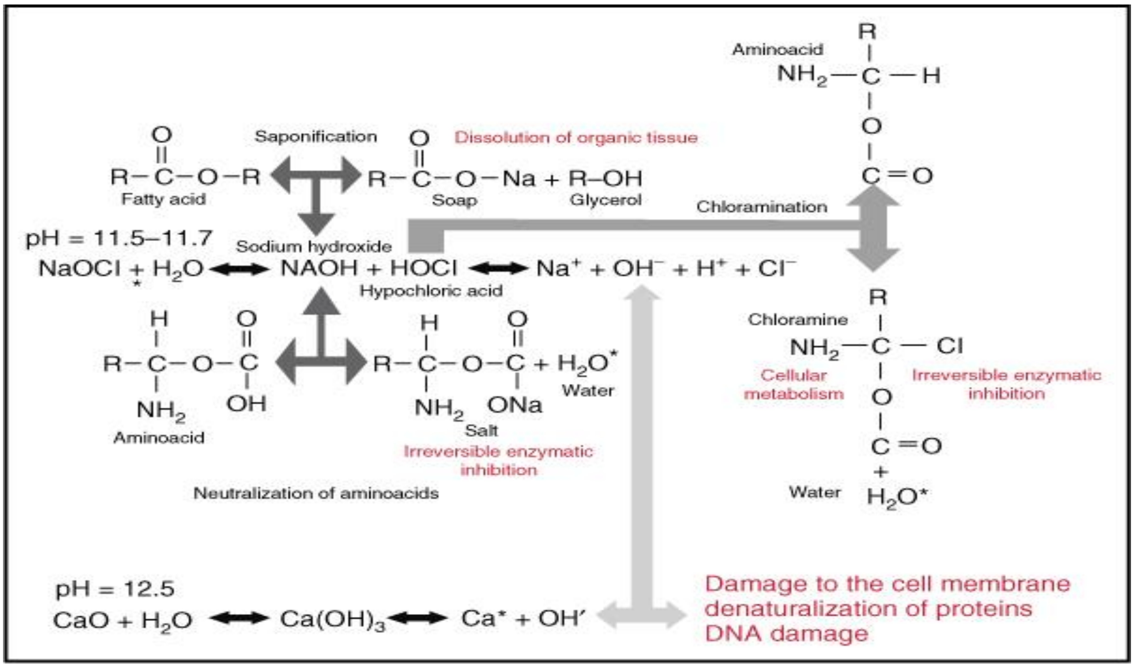
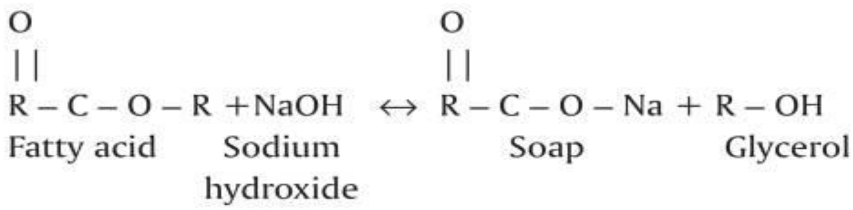
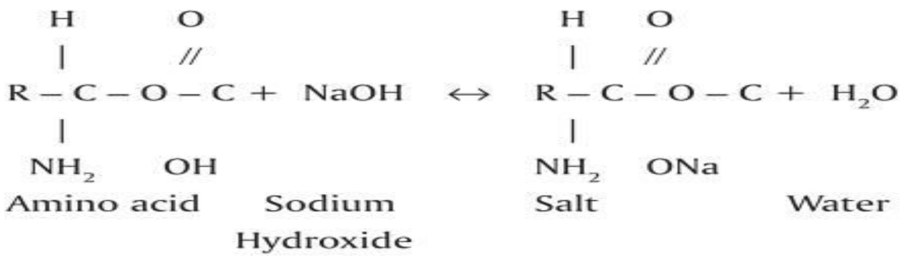


Figure 2: Schematic diagram of the mechanism of action of NaOCl, courtesy Dr. A. Manzur (Kenneth Hargreaves Louis Berman, 2015)

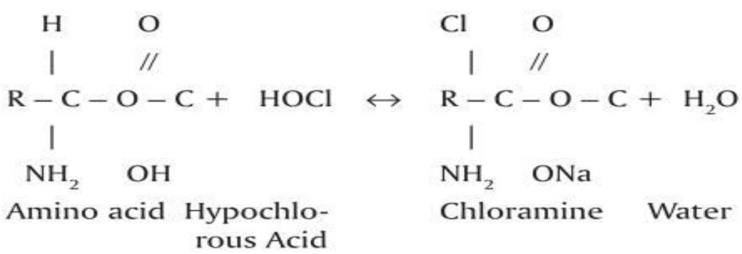
1) **Saponification:** Interpreting these chemical reactions, sodium hypochlorite acts as a solvent for organic and fat degrading fatty acids, transforming them into fatty acid salts and glycerol (alcohol) that reduces the surface tension of the remaining solution.



2) **Neutralization**: Sodium hypochlorite neutralizes amino acids forming water and salt (neutralization reaction) with the exit of hydroxyl ions, there is a reduction in pH.



3) Hypocblorous acid formation: a substance present in sodium hypochlorite solution, when in contact with organic tissue and water acts as a **solvent** and releases chlorine gas, combined with the protein amino group, forms chloramines (chloramination reaction) that interfere in cell metabolism. Hypochlorous acid ($HOCl^-$) and hvpochlonte ions (OCl^-) lead to amino acid degradation and hydrolysis. Chlorine (a strong **oxidant**) presents antimicrobial action inhibiting bacterial enzymes leading to an irreversible oxidation of SH groups (sulfydryl group) of essential bacterial enzymes. Considering the chemico-physical properties of sodium hypochlorite when in contact with organic tissue, these reactions can be verified.



4) **High pH**: Sodium hypochlorite is a strong base (pH>11). At 1% concentration, sodium hypochlorite presents a surface tension equal to 75 dynes/cm, stickiness equal to 0.986 cP, conductivity of 65.5 mS, density of l.04g/cm3 and moistening capacity equal to 1h and 27min. Its antimicrobial mechanism of action can be

observed verifying its chemico-physical characteristics and its reaction with organic tissue.

It has a noticeable effect on biofilm, according to (Kandaswamy & Venkateshbabu, 2010):

1. Complete dissolution of cells with absence of visual evidence
2. Bacterial cells are disrupted and separated from the biofilm and are nonviable
3. Bacterial cells remain adherent within the biofilm but are nonviable
4. Bacterial cells are disrupted and separated from the biofilm but are viable
5. Bacterial cells remain adherent within the biofilm and are still viable

The antimicrobial effectiveness of sodium hypochlorite, based in its high pH (hydroxyl ions action), is similar to the mechanism of action of calcium hydroxide (Zehnder, 2006). The ability of NaOCl to dissolve both necrotic and vital tissue is effected by concentration , time, temperature, tissue contact irrigant area, canal preparation size, volume , tissue type and mechanical action (Christensen, McNeal, & Eleazer, 2008).

B) Chlorhexidine: CHX is a strong basic molecule with a pH between 5.5 and 7 that belongs to the polybiguanide group and consists of two symmetric four-chlorophenyl rings and two bisbiguanide groups connected by a central hexamethylene chain (Figure 3). CHX digluconate salt is easily soluable in water and very stable (Shreya, 2016).

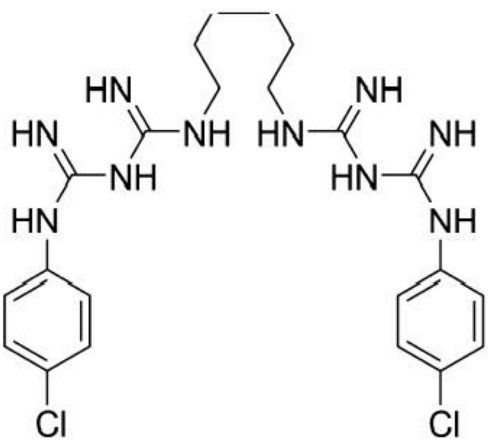


Figure 3: Molecular structure of chlorhexidine (B. Basrani & Haapasalo, 2012)

Mode of action:

1. As an antimicrobial agent: The mechanism of action is found to take place through the cationic ions that are negatively charged. They rapidly gets attracted to the inner cell membrane of the bacteria and other microbes, rendering it permeable and exerts bactericidal effect to eliminate them thus serving as an antiplaque and antimicrobial agent (Basrani, B. 2005).
2. Substantivity of chlorhexidine : Chlorhexidine offers oral retentivity as it's capable of absorbing the negativity charged surfaces in tooth , mucosa, pellicle, restorative materials and other oral structures .Recent studies on the substantive nature of chlorhexidine has reported on the inhibition of dentinal proteases thereby prolonging the durability of resin dentin bonds, especially in the absence of collagen (Shreya, 2016); (Davies, 1973).

C) Decalcifying agents: Debris is defined as dentine chips or residual vital or necrotic pulp tissue attached to the root canal wall. Smear layer is defined by the American Association of Endodontics in 2003 as "A surface film of debris retained on dentin or another surface after instrumentation with either rotary instruments or endodontic files; it consist of dentine particles, remnants of vital or necrotic pulp tissue, bacterial components and retained irrigants" Although it has been viewed as an impediment to irrigant penetration into dentinal tubules , there is still a controversy about the influence of smear layer on the outcome of endodontic treatment (Kenneth Hargreaves Louis Berman, 2015).

Until recently, decalcifying solutions in endodontics were only comprised of chelators and acids, most commonly EDTA and citric acid. In the last few years, however, several combination products have appeared where their main function—that is, their decalcifying effect—has been combined with other characteristics thought to be helpful for treatment. The added characteristics are reduced surface tension and, perhaps more importantly, antibacterial activity. The new combination products are based either on EDTA or citric acid. Both NaOCl and a decalcifying agent are required for complete removal of the smear layer for the organic and inorganic matrix respectively. In addition to weak acids, solutions for the removal of the smear layer include carbamide peroxide, aminoquinaldinium diacetate (i.e. Salvizol), and EDTA. In objective studies, carbamide peroxide and Salvizol appear to have little effect on smear layer buildup. We will try in this study to focus on EDTA since the other decalcifying agents are relatively new and/or not as potent neither widely used as EDTA, alongside with Qmix for its unique nature, until more studies are concluded about the efficacy of the new products.

Results and discussion: The chemical interaction between endodontic irrigants:

1) NaOCl and CHX

Comparing to NaOCl, CHX has a low level of tissue toxicity, locally and systemically, and using the combination has a further reduction in the proportion of positive cultures and a better disinfection of root canals (Zamany, Safavi, & Spångberg, 2003), in another study of (Kuruvilla & Kamath, 1998); CHX was found to be as effective as NaOCl or possibly more effective in its antimicrobial property when compared with sodium hypochlorite irrigants. These irrigants significantly reduced the post-irrigant positive cultures and colony forming units when compared with the saline irrigated teeth. The results from the individual trial of chlorhexidine gluconate and sodium hypochlorite indicate that they are equally effective antibacterial agents. However, when these solutions were combined within the root canal, the antibacterial action was suggestive of being augmented. The possible reason for this could be due to the following reaction:

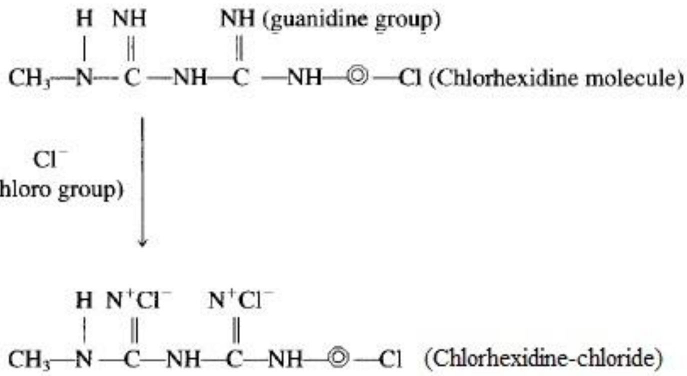
Chlorhexidine is a base, capable of forming salts with a number of organic acids solely with the organic matrix. In the other hand, sodium hypochlorite is an oxidizing agent that may be capable of oxidizing the gluconate part of chlorhexidine to gluconic acid. The chloro groups might get added on to the guanidine component of the chlorhexidine molecule, thereby forming "chlorhexidine-chloride." This reaction may be depicted as follows:

I. $NaOCl + H_2O$------$NaOH + HOCl$

$HOCl$-----------------$HCl + [O]$

HCl-------------------H^+Cl^-

II.



If this were to happen, it would increase the ionizing capacity of the chlorhexidine molecule, and the solution would incline toward an alkaline pH. This was evident when the pH of sodium hypochlorite solution, chlorhexidine gluconate solution, and their combination were recorded using a pH meter. The pH was recorded as follows: In 2.5% NaOC1 pH was {9} and in 0.2% Chlorhexidine Gluconate pH was {6.5}. However, with the Combination of both pH recorded as {10}. It is a known fact that the ionized species exert better antibacterial action than the unionized species The study emphasize the fact that further studies to validate the above findings would be of interest. This study conforms to the findings of others who have previously evaluated the antibacterial properties of sodium hypochlorite and CHX as endodontic irrigants.

In another study done by (Ng, Mann, & Gulabivala, 2011) , they concluded that using the combination of both (NaOCl-CHX) has a lower periapical healing and reduced the success of treatment by 53%. This finding did not support previous reports (Siqueira, Magalhães, & Rôças, 2007); (Zamany et al., 2003) on its equivalent or superior *in vivo* antibacterial efficacy when compared with sodium hypochlorite. The negative impact of using alternate irrigation with sodium hypochlorite and chlorhexidine solution on root canal treatment outcome may be attributed to their interaction product. It is an insoluble precipitate containing para-chloro-aniline (PCA), which is cytotoxic and carcinogenic (B. R. Basrani, Manek, Sodhi, Fillery, & Manzur, 2007). The interaction may mutually deplete the active moieties for bacterial inactivation, whilst the precipitate may cause persistent irritation to the periapical tissue, as well as block dentinal tubules and accessory anatomy. Given the nonrandomized nature of this study, they argue that the results may be confounded by the fact that chlorhexidine was only used in cases with persistent weeping canals, soft-tissue swelling, pain or sinus tract following chemo-mechanical debridement using NaOCl as an irrigant and $Ca(OH)_2$ as an inter-appointment medicament. The potential correlations between the supplementary use of chlorhexidine and these clinical conditions had been explored, and no significant correlation was found. In addition, the prognostic value of this factor remained significant at the 5% level even after accounting for these clinical conditions (presence of preoperative sinus, presence and size of periapical lesion, and presence of interappointment flare-up). The present findings should therefore be considered as sufficiently robust, although the effect of the supplementary use of chlorexidine should be further investigated in a randomized controlled trial (Ng et al., 2011).

This precipitate, was studied thoroughly in the study of (Prado et al., 2013) which evaluated the by-products formed in the association between the irrigants commonly used in endodontic treatment, represented in (Table1). In that study, the association of NaOCl at concentrations of 1%–5.25% with 2% CHX solution and gel resulted in orange-brown precipitates (Fig. 4*A*). The mass spectrometry analyses confirmed the presence of several products of chlorination from the oxidizing agent NaOCl, which occurs at 1 to 6 guanidino nitrogens of CHX. The orange-brown color can be associated with the guanidine oxidation. Their findings were in accordance with those of (Nowicki & Sem, 2011; Thomas & Sem, 2010) who did not find the presence of *para*-chloroaniline by using nuclear magnetic resonance.

However, their results diverge from the results of (B. R. Basrani et al., 2007), who found it by using x-ray photon spectroscopy and time-of-flight secondary ion mass spectrometry. The different results may be due to the differences between the techniques. TOF secondary ion mass spectrometry deals with surface analyses (similar to x-ray photon spectroscopy) and has a different mechanism of transferring molecules or their aggregates into the mass spectrometer. On the other hand, by using nuclear magnetic resonance or ESI-QTOF-MS, the precipitate is all dissolved in a solvent, and afterwards, the solution is analyzed. Besides the difference between these techniques, the comparison of the mass spectrometry results obtained by the different research groups is not possible, because the MS spectra have not been fully described in the literature yet.

The 0.16% NaOCl was evaluated to verify whether a much diluted NaOCl solution would produce a chemical precipitate in the presence of CHX. The orange-white precipitate formed was attributed to the lower concentration of NaOCl. Regarding the attributed results (Fig. 4*B*). only the chemical structure of the CHX chlorinated at 1, 2, and 3 guanidino nitrogens was found, but nothing on its toxicity (Anborn & Ammock, 1999), (Prado et al., 2013). This compound is a very potent inhibitor of the human enzyme soluble epoxide hydrolase (inhibitory concentration of 50% = 1.05 ± 0.03), which can be used to selectively inhibit epoxide hydrolase in therapeutic applications (eg, inflammation treatment, affinity separations of the epoxide hydrolases) and in conjunction with cancer therapy, according to Anborn & Ammock, 1999.

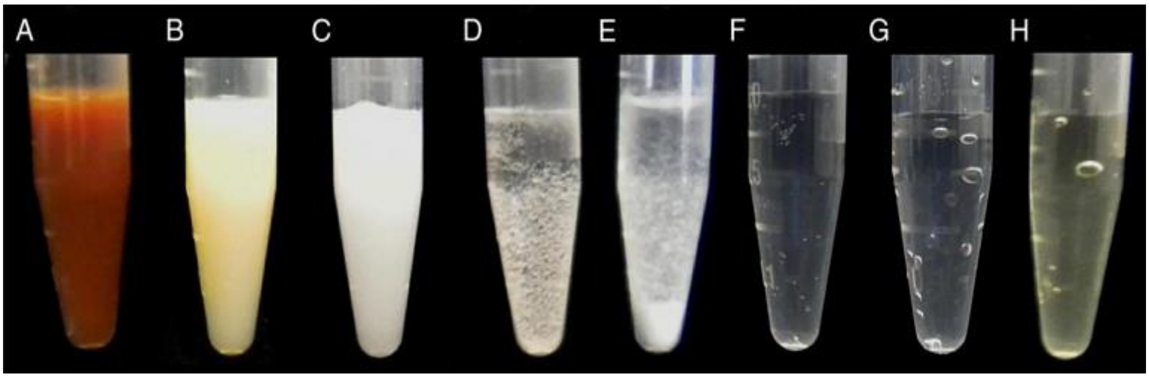


Figure 4: Visual aspect of the interactions between the following: (*A*) 5.25% NaOCl and 2% CHX; (*B*) 0.16% NaOCl and 2% CHX; (*C*) 17% EDTA and 2% CHX; (*D*) saline solution and 2% CHX; (*E*) ethanol and 2% CHX; (*F*) 5.25% NaOCl and 17% EDTA; (*G*) 5.25% NaOCl and 10% citric acid; (*H*) 5.25% NaOCl and 37% phosphoric acid. (Prado et al., 2013)

Entry	Solution 1	Solution 2	Appearance of the resultant association*
1	2% CHX gel	5.25% NaOCl	Orange-brown precipitate
2	2% CHX gel	2.5% NaOCl	Orange-brown precipitate
3	2% CHX gel	1% NaOCl	Orange-brown precipitate
4	2% CHX gel	0.16% NaOCl	Orange-white precipitate
5	2% CHX gel	17% EDTA	White milky precipitate
6	2% CHX gel	10% Citric acid	Unchanged
7	2% CHX gel	37% Phosphoric acid	Unchanged
8	2% CHX gel	Distilled water	Unchanged
9	2% CHX gel	Saline solution	Salt precipitation
10	2% CHX gel	Ethanol	Salt precipitation
11	2% CHX solution	5.25% NaOCl	Orange-brown precipitate
12	2% CHX solution	2.5% NaOCl	Orange-brown precipitate
13	2% CHX solution	1% NaOCl	Orange-brown precipitate
14	2% CHX solution	0.16% NaOCl	Orange-white precipitate
15	2% CHX solution	17% EDTA	White milky precipitate
16	2% CHX solution	10% Citric acid	Unchanged
17	2% CHX solution	37% Phosphoric acid	Unchanged
18	2% CHX solution	Distilled water	Unchanged
19	2% CHX solution	Saline solution	Salt precipitation
20	2% CHX solution	Ethanol	Salt precipitation
21	5.25% NaOCl	17% EDTA	Bubble formation
22	5.25% NaOCl	10% Citric acid	Bubble formation
23	5.25% NaOCl	37% Phosphoric acid	Yellow solution with bubble formation
24	5.25% NaOCl	Distilled water	Unchanged
25	5.25% NaOCl	Saline solution	Unchanged
26	5.25% NaOCl	Ethanol	Unchanged
27	2.5% NaOCl	17% EDTA	Bubble formation
28	2.5% NaOCl	10% Citric acid	Bubble formation
29	2.5% NaOCl	37% Phosphoric acid	Yellow solution with bubble formation
30	2.5% NaOCl	Distilled water	Unchanged
31	2.5% NaOCl	Saline solution	Unchanged
32	2.5% NaOCl	Ethanol	Unchanged
33	1% NaOCl	17% EDTA	Bubble formation
34	1% NaOCl	10% Citric acid	Bubble formation
35	1% NaOCl	37% Phosphoric acid	Slight yellow solution with bubble formation
36	1% NaOCl	Distilled water	Unchanged
37	1% NaOCl	Saline solution	Unchanged
38	1% NaOCl	Ethanol	Unchanged
39	0.16% NaOCl	17% EDTA	Unchanged
40	0.16% NaOCl	10% Citric acid	Unchanged
41	0.16% NaOCl	37% Phosphoric acid	Unchanged
42	0.16% NaOCl	Distilled water	Unchanged
43	0.16% NaOCl	Saline solution	Unchanged
44	0.16% NaOCl	Ethanol	Unchanged

Table 1: Association of irrigants and visual characteristic of the products.
*Solution 1 and Solution 2 mixed in 1:1 ratio (Prado et al., 2013)

In the study of B. R. Basrani, Manek, & Fillery, 2009, with the aim to use a diazotization technique to confirm the presence of an aromatic amine (like PCA) in the NaOCl/CHX precipitate and also in the 2.0% CHX at different temperatures (37°C and 45°C).The end products of the PCA, the NaOCl/CHX precipitate, and 2.0% CHX at 45°C were yellow, indicating that an aromatic amine was present in all samples. However, CHX at room temperature or heated at 37°C turned white, indicating that no aromatic amine was present. Considering that CHX can break down to form PCA by exposure to heat, this study was designed to verify the formation of PCA in heated CHX. In a clinical situation, ultrasonic energy is recently advocated as a means of removal of the smear layer and bacteria from the root canal (Cameron JA. 1988). Although till to date no studies have shown an enhanced antibacterial effect of the combination of CHX and ultrasonic energy, it is conceivable that clinicians who use CHX might consider using vibration to enhance the distribution and effect of the irrigant within the root canal. It has been shown that ultrasonic activation might increase the temperature to at least 45°C. Heated CHX at 45°C displayed the possible formation of PCA; therefore, ultrasonic activation of CHX should be avoided until further investigation is done (Cameron JA. 1988).

Another study by the same author; Basrani and his colleagues (B. R. Basrani et al., 2007) recommended to reduce the formation of the precipitate 4-chloronaline (PCA) by removing the NaOCl before placing the CHX; using flushes of saline water followed by paper points to dry the canals out. Using paper points, or air dry, or saline or citric acid, just reduced the precipitate formation. It has been suggested to use citric acid before the rinse with CHX, and this allowed Dentine Tubules to remain open without the formation of precipitate (Akisue et al 2010). However, PCA is still present after this regimen (Mortenson 2012). Distilled water is also suggested as another irrigant to prevent or at least reduce the formation of the precipitate (Prado 2013). If saline or distilled water are used before CHX, then the thickness of the precipitate is decreased compared to the dentin where intermediate irrigation is not used. Ethanol, on the other hand, completely eliminates the formation of the precipitate, as determined by a visual inspection method (Krishnamurthy 2010).

On the other hand, in the study of Bui, Baumgartner, & Mitchell, 2008, which aimed to study the effect of the interaction between CHX and NaOCl on dentine tubules, they concluded that the precipitate affected significantly the patency of the dentinal tubules. There were 4 groups: **Group A**: The canal was left filled with 5 mL of NaOCl 5.25%. Then 5 mL 2% CHX was used as a final irrigant followed by immediately drying of the canal with paper points. **Group B**: 5 mL of 5.25% NaOCl was used to irrigate and then aspirated and immediately dried with paper points from canal. A final irrigation with 5 mL 2% CHX was done. **Group C**: (Negative Control): A final irrigation with 5 mL 5.25% NaOCl was performed. The canal was aspirated and dried with paper points. **Group D**: (Positive Control): A final irrigation of 5 mL 5.25% NaOCl was performed. The canal was left flooded and allowed to air dry under cover at room temperature. There was a statistically significant reduction in the number of patent dentinal tubules in the 2 experimental groups when compared with the negative control group. They found the following results represented in (Table 2):

1. The interaction with CHX did not leave behind a significant amount of gross precipitate on the root canal surface when NaOCl was aspirated and dried with paper points, and even when it was left flooded in the root canal,,

2. There were no significant differences in the percentage of remaining debris between the groups, neither.

3. The interaction between CHX and NaOCl, however, affected significantly the patency of the dentinal tubules by coating the root surface. There was a statistically significant reduction in the number of patent dentinal tubules in the 2 experimental groups when compared with the negative control group. Removing NaOCl by aspiration and paper points showed no significant

reduction to this affect. Apparently, the dentin and its tubules harbor enough residual NaOCl that it reacts with the CHX in the canal. This indicates that a small amount of the precipitate is left behind and raises potential concerns with respect to leaching of the precipitate into the surrounding tissues and the seal of the root canal.

4. The obliteration of dentinal tubules was not found to be significant at the apical third. There were no significant differences between all experimental and control groups. He referred that it might be due to the fact that the apical third is more difficult to irrigate. Results at the apex might have been different if irrigation was supplemented with sonic, ultrasonic, or negative pressure irrigation. Because the coronal and middle thirds are significantly affected, these results remain a concern. Examination of the ESEM micrographs revealed a subjective change in the morphology of the root surface (Figure 5). The use of NaOCl and CHX appears to coat the root surface. The substance coating the root surface and obliterating the dentinal tubules was not identified.

Root location	Mean ± SD			
	Group A (maximum precipitate produced)	Group B (minimum precipitate produced)	Group C (negative control)	Group D (positive control)
Coronal third	102.33 ± 41.40	87.93 ± 54.14	151.00 ± 29.16	44.29 ± 45.58
		P < 0.05		
		P < 0.05		
			P < 0.05	
		P < 0.05	P < 0.05	
Middle third	15.93 ± 19.40	39.60 ± 38.83	65.71 ± 17.71	24.57 ± 20.85
	P < 0.05			
		P < 0.05		
		P < 0.05	P < 0.05	
Apical third	16.80 ± 21.82	11.20 ± 16.47	21.29 ± 16.79	16.57 ± 15.99

TABLE 2: Number of Patent Tubules per 4843 μm^2. SD, standard deviation. Statistically significant differences are indicated with *P* values. There were 4 groups: Group A: The canal was left filled with 5 mL of NaOCl 5.25%. Then 5 mL 2% CHX was used as a final irrigant followed by immediately drying of the canal with paper points. Group B: 5 mL of 5.25% NaOCl was used to irrigate and then aspirated and immediately dried with paper points from canal. A final irrigation with 5 mL 2% CHX was done. Group C: (Negative Control): A final irrigation with 5 mL 5.25% NaOCl was performed. The canal was aspirated and dried with paper points. Group D: (Positive Control): A final irrigation of 5 mL 5.25% NaOCl was performed. The canal was left flooded and allowed to air dry under cover at room temperature to air dry under cover at room temperature. From our pilot study, crystalline debris was found under the SEM when a canal was flooded with NaOCl and left to dry. (Bui et al., 2008)

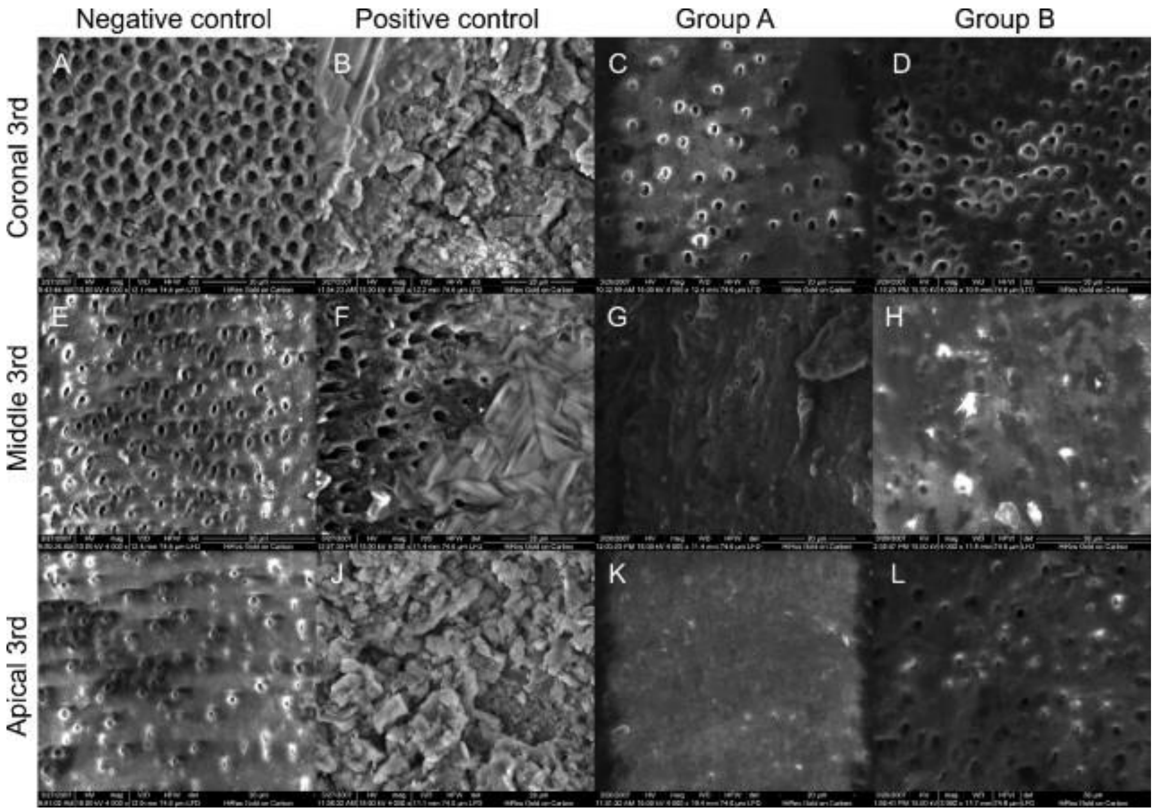


Figure 5: Representative SEM micrographs of root surfaces at 4000×. Negative control group shows no obvious debris and complete removal of smear layer. Presence and diameter of patent dentinal tubules decline in number from the coronal to the apical third. Positive control shows gross amounts of debris that obscure the dentinal tubules in all root thirds. Experimental groups do not show any obvious debris. However, the dentinal tubules appear obliterated especially in the middle third. Subjectively, the experimental groups root surfaces appear to be coated with unidentified material. (Bui et al., 2008)

In another study (Vivacqua-Gomes et al., 2002) aimed to assess in vitro the coronal microleakage in extracted human teeth after root-canal treatment laterally condensed with gutta-percha, using different endodontic irrigants, demonstrated by Table3. The teeth from Group II (1% NaOCl + 17% EDTA) had the least leakage (mean 2.62 mm) followed by Group III (2% CHX gel) (mean 2.78 mm); there was no significant deference between the two groups. The mean coronal microleakage of teeth from Group I (1% NaOCl) (mean 3.51 mm) was significantly greater than in Groups II and III ($P < 0.05$). Group IV (2% CHX gel + 1% NaOCl) had the most leakage (mean 9.36 mm) that was significantly deeper ($P < 0.05$) even when compared to the teeth irrigated with Group V (distilled water) (mean 6.10 mm). During irrigation of Group IV teeth, the formation of a marked dark-brown precipitate was observed, resulting from the combination of 2% CHX gel with 1% NaOCl. Even after the final flush with distilled water the precipitate could be observed staining the dentine.

Groups	Mean leakage (mm)	SD	Range (mm)
I (1% NaOCl)	3.51[b]	1.31	1.6–7.00
II (1% NaOCl + 17% EDTA)	2.62[a]	0.96	1.26–5.3
III (2% chlorhexidine gel)	2.78[a]	1.41	0.3–5.15
IV (2% chlorhexidine gel + 1% NaOCl)	9.36[d]	1.69	6.00–12.00
V (distilled water)	6.10[c]	2.28	2.88–12.00

Mean followed by the same letter are not significantly different ($P \geq 0.05$).

Table 3: Coronal linear dye penetration after irrigation regimes and obturation. (Vivacqua-Gomes et al., 2002)

2) NaOCl and EDTA

The findings on the additional use of 17% EDTA solution after NaOCl for irrigation were previously unreported. Its use had a marginal effect on the success of primary treatment (OR = 1.3 [0.8, 2.1]) but had a profound effect on secondary treatment (OR = 2.3 [1.4, 3.8]). The long-term (≥2 years) outcome of their cases stratified by various canal disinfection protocolswas not consistent with their microbiological findings. The percentage of teeth with periapical healing for alternate irrigation with sodium hypochlorite and EDTA solutions was low (67%) when compared with that for irrigation using saline (91%), 0.5% sodium hypochlorite (92%) or 5% sodium hypochlorite (86%). Their outcome data were unexpected as preobturation negative bacterial culture was achieved in all cases. However, given the comprehensive microbiological investigations involved, each group consisted of only 11–15 teeth; these clinical outcomes should therefore be interpreted with caution. The synergistic effect of the two agents is attributed to their combined effects on inorganic and organic components within the root canal system. The actions of EDTA include its chelating properties, which assist in negotiation of narrow or sclerosed canals by demineralization of root dentine and help remove compacted fibrous tissue from un-instrumented canal anatomy. It may also facilitate deeper penetration of sodium hypochlorite solution into dentine by removing the smear layer from the instrumented surface and opening up dentinal tubules, and lastly it may help detach or breakup adherent biofilms by chelating heavy metals ions that help to bind bacterial cells together in the biofilm (Gulabivala, Patel, Evans, & Ng, 2005). In 2°RCTx cases, the previously treated canals may contain contaminated debris, smear layer, un-negotiable calcifications or iatrogenic blockages, and lastly bacterially contaminated filling material. The additional use of EDTA irrigation may help by aiding removal of such contaminated materials and opening up accessory anatomy and blocked canal exits. In contrast, the smear layer and debris generated from instrumentation of previously untreated canals during 1°RCTx should be more accessible to and relatively easily decontaminated by sodium hypochlorite solution alone. This may possibly explain why the success of 1°RCTx was not significantly improved by additional EDTA irrigation, whilst that of 2°RCTx was (Gulabivala et al., 2005)

In the study of Grawehr, Sener, Waltimo, & Zehnder, 2003, Ethylenediamine tetraacetic acid showed that it retained its calcium-complexing ability when mixed with NaOCl, but EDTA caused NaOCl to lose its tissue-dissolving capacity and virtually no free chlorine was detected in the combinations. Clinically, this suggests that EDTA and NaOCl should be used separately. In an alternating irrigating regimen, copious amounts of NaOCl should be administered to wash out remnants of the EDTA. An EDTA solution maintained its calcium-chelating ability and its anti-microbial effectiveness when combined with NaOCl. However, NaOCl lost available chlorine and therefore its tissue-dissolving effectiveness when EDTA was added (Table 4).

	Enterococcus faecalis ATCC 29212	*Candida albicans* OMZ 110
Saline	0	0
NaOCl 0.5%	1.3 ± 0.3^a	1.5 ± 0.0
EDTA 8.5%	3.0 ± 1.0	9.8 ± 0.3
EDTA 17% and NaOCl 1% (1 : 1)	3.0 ± 1.3	9.8 ± 0.3

[a]Mean value ± SD ($n = 3$).

Table 4: Zones on inhabitation (mm) vs tests organisms (agar diffusion) (Grawehr et al., 2003)

In the study of Baumgartner & Ibay, 1987, using a Universal Gas Sampler with a Chlorine Indicator Tube (Bacharach, Pittsburgh, PA) to determine if chlorine gas emission, which is very irritating to mucous membranes, eyes and respiratory tract, is evolved when NaOCl is combined with H_2O_2, EDTA and citric acid (Table 5), it concluded that:

1. No chlorine could be detected when NaOCl was used alone or with combination with water
2. Chlorine was detected at a level of <0.5 ppm when NaOCl 5.25% in conjunction with 15% EDTA
3. Chlorine was detected at a level of 3.5 ppm when NaOCl 5.25% in conjunction with 50% citric acid
4. The combination of NaOCl and EDTA seems to have all the capabilities of NaOCl and Citric acid without as much chlorine being involved during root canal therapy. Thus, NaOCl and EDTA would be the combination of choice if

the Dentist wishes to remove both organic and inorganic from root canal system during chemomechanical debridement.

ppm	
1	Slight symptoms after several hours
3.5	Concentration detectable by odor
4	Maximum concentration that can be breathed for 1 h without damage
15	Concentration causing throat irritation
50	Concentration dangerous in 30 min
1000	Fatal after a few breaths

Table 5: Effects of chlorine on man (Baumgartner & Ibay, 1987)

The results had been confirmed later by the study of (Prado et al., 2013) when NaOCl was mixed with EDTA, citric acid, or phosphoric acid, an exothermic reaction with formation of bubbles was observed. The presence of bubbles was most intense for phosphoric acid, followed by citric acid and finally the less intense was for EDTA. These bubbles are mainly chlorine gas, a toxic product. The bubble formation of chlorine gas (Cl_2) results from an increase in proton (H^+) concentration in the presence of chloride ions (Cl^-), which is the usual impurity of NaOCl solutions, shifting the equilibrium toward the formation of Cl_2. In addition, it can also be produced by the oxidation of EDTA or citric acid by HOCl.

3) CHX and EDTA

The combination of CHX and EDTA produce a white precipitate as shown in (Figure 6), so a group of investigators (Rasimick, Nekich, Hladek, Musikant, & Deutsch, 2008) did a study to determine whether the precipitate involves the chemical degradation of CHX. The precipitate was produced and dissolved in a known amount of dilute triflouracetic acid. Based on the result, CHX was found to form a salt with EDTA rather than undergoing a chemical reaction. The clinical significance of the EDTA/CHX precipitate is largely unknown. There are no published measurements of how much precipitate adheres to the root canal dentin. Furthermore, it is unknown if any adhering precipitate interferes with the apical seal. The present study is valuable because it shows that the reaction between CHX and EDTA, unlike the reaction between CHX and NaOCl, does not produce significant quantities of p-chloroaniline.

In the study of Prado et al., 2013 the white milky precipitate produced in the association of EDTA with CHX solution and gel was analyzed by ESI(+)-MS and found to be related to the acid-base reactions. The data were in accordance with those of

Rasimick et al., 2008, who analyzed the precipitate formed after mixing 17% EDTA with 2% or 20% CHX by using reversed-phase high-performance liquid chromatography and observed that more than 90% of the precipitate mass was either EDTA or CHX salt. The precipitate formed between CHX and saline solution was attributed to the salting-out process, the introduction of saline solution increased the concentration of salt and precipitated the CHX salts, whereas the precipitate formed between CHX and ethanol was attributed to the reduced solubility of the CHX salt in ethanol.

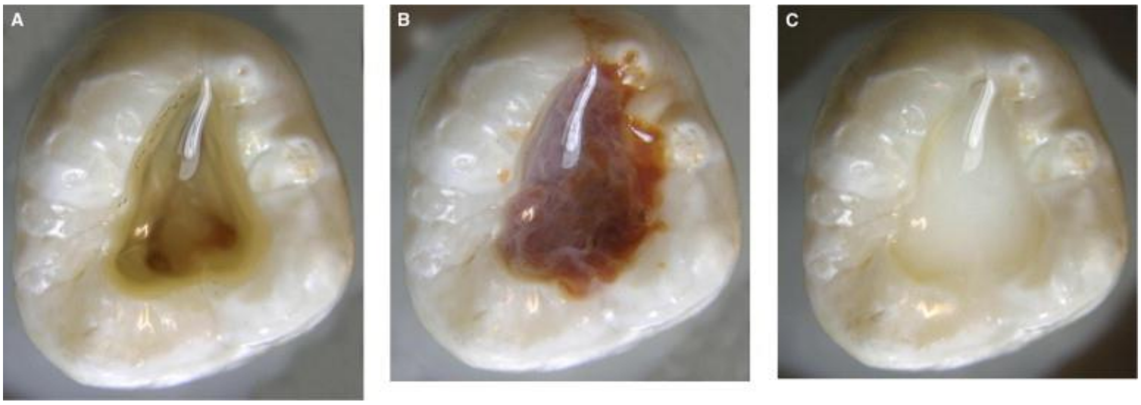


Figure 6: Extracted teeth with endodontic access cavities containing CHX mixed with various irrigants. (*A*) Water, (*B*) NaOCl, and (*C*) EDTA. Note that NaOCl and EDTA cause CHX to form a precipitate. (Rasimick et al., 2008)

4) QMiX®

QMiX was introduced in 2011; it's recommended to be used at the end of instrumentation, after NaOCl irrigation, as a final rinse. According to the patent, QMiX contain a CHX-analog, Triclosan and EDTA as a decalcifying agent, it's intended to be an antimicrobial irrigant as well as an agent to remove canal wall smear layer and debris. And because of its unique nature, which has the potential contact between the three dominant irrigants in endodontic (NaOCl with EDTA+CHX) it's included as another example of the decalcifying agent.

In the study of Arslan et al., 2015 who used a 400-MHz Bruker NMR System to measure the spectra of the precipitate; Chlorhexidine had significantly higher scores than QMiX in terms of orange-brown precipitate formed in the root canals ($P < 0.001$). According to the 1H NMR spectra, para-chloroaniline was present in the mixture of chlorhexidine and NaOCl. However, the mixture of QMiX and NaOCl did not result in para-chloroaniline formation. These results were confirmed by Kolosowski, Sodhi, Kishen, & Basrani, 2014, when no precipitate or PCA was detected in the tubules of dentin irrigated with NaOCl followed by saline and QMiX, by using time-of-flight secondary ion mass spectrometry (TOF-SIMS).

Time	Sterile water	2% NaOCl	6% NaOCl	2% CHX	QMiX
1 min					
1 d	0.03 ± 0.01^{a}	0.25 ± 0.11^{c}	0.44 ± 0.13^{e}	0.24 ± 0.08^{c}	0.46 ± 0.10^{e}
3 w	0.04 ± 0.02^{a}	0.15 ± 0.07^{b}	0.35 ± 0.08^{d}	0.13 ± 0.05^{b}	0.26 ± 0.10^{c}
3 min					
1 d	0.05 ± 0.03^{a}	0.35 ± 0.12^{d}	0.61 ± 0.10^{f}	0.36 ± 0.12^{d}	0.61 ± 0.11^{f}
3 w	0.05 ± 0.02^{a}	0.25 ± 0.08^{c}	0.54 ± 0.17	0.26 ± 0.11^{c}	0.40 ± 0.11^{de}

Table 6: Proportion of Dead E. faecalis Cell Volume in the Dentinal Tubules Exposed to Different Disinfecting Solutions after 1-Day and 3-Week Incubation (Wang Z, Shen Y, 2012)

In the study of Stojicic, Shen, Qian, Johnson, & Haapasalo, 2012 which investigated the effectiveness of removal of smear layer by QMiX by using SEM and they concluded that its ability of removing of smear layer is equally well as EDTA. They also studied the efficacy against E.faecalis and mixed plaque bacteriain planktonic phase and biofilms, QMiX and 2% NaOCl killed up to 12 times more of the biofilm bacteria than 1% NaOCl, and killed all planktonic E.faecalis and plaque bacteria in 5 seconds. Several studies (Morgental et al., 2013); (Wang Z, Shen Y, 2012) concluded that 6% NaOCl and QMiX were the most effective vs young biofilm whereas vs 3 weeks old biofilm , NaOCl was the most effective followed by QMiX , 2% NaOCl and lastly came 2% CHX. Although these studies were done in vitro and mostly with little number of test objects, we must consider the fact that QMiX is still relatively new and more studies should be done regarding its anti-microbial effect before considering using it solely, and till then we should use it as intended, as a final rinse after NaOCl irrigation.

Conclusions:

Irrigation plays a key role in the success of endodontic treatment. The main goal of root canal treatment is to completely eliminate the different components of pulpal tissue, bacteria, and biofilm and produce a hermetic seal to prevent infection or reinfection and promote healing of the surrounding tissues. The extra time we gain by using rotary NiTi instruments should be used for abundant irrigation to achieve better cleaning of the root canal system, thereby contributing to improved success of the treatment. The most commonly used irrigating solution is sodium hypochlorite. While sodium hypochlorite has many desirable qualities and properties, by itself it is not sufficient to totally clean the root canal system of organic and inorganic debris and biofilm. For optimal irrigation, a combination of different irrigating solutions must be used.

The dentist should be aware of the interactions between the various chemicals found in irrigants as they may weaken each other's' activity and result in the development of products that are harmful to the host. The most worrying by-product is the orange-brown precipitate (PCA) observed in the association between CHX and NaOCl because of its cytotoxicity, resistance to be removed, ability to occlude the dentine canals, micro leakage and failure of the endodontic treatment accordingly. NaOCl and EDTA led mainly to chlorine gas formation which seemed to be within the tolerable range. The less undesirable reaction was from CHX with EDTA and was less harmful to endodontic treatment, resulted in white precipitate which was associated with acid-base reaction. QMiX is safe to use and no PCA was detected when followed NaOCl as final rinse. The majority of the studies suggest that intermediate flushes with distilled water seem to be appropriate to prevent or at least reduce the formation of the by-products, with the exception of PCA formation from (NaOCl-CHX) reaction.

Developing a rational irrigation sequence so that the chemicals are administered in a proper manner to release their full potential is imperative for successful endodontic treatment. A suggested irrigation protocol (B. Basrani & Haapasalo, 2012) is presented in Figure 7 and is highly advisable, with only one modification which is to use Ethanol instead of saline as a rinse between CHX & NaOCl (Krishnamurthy 2010), until more studies are done.

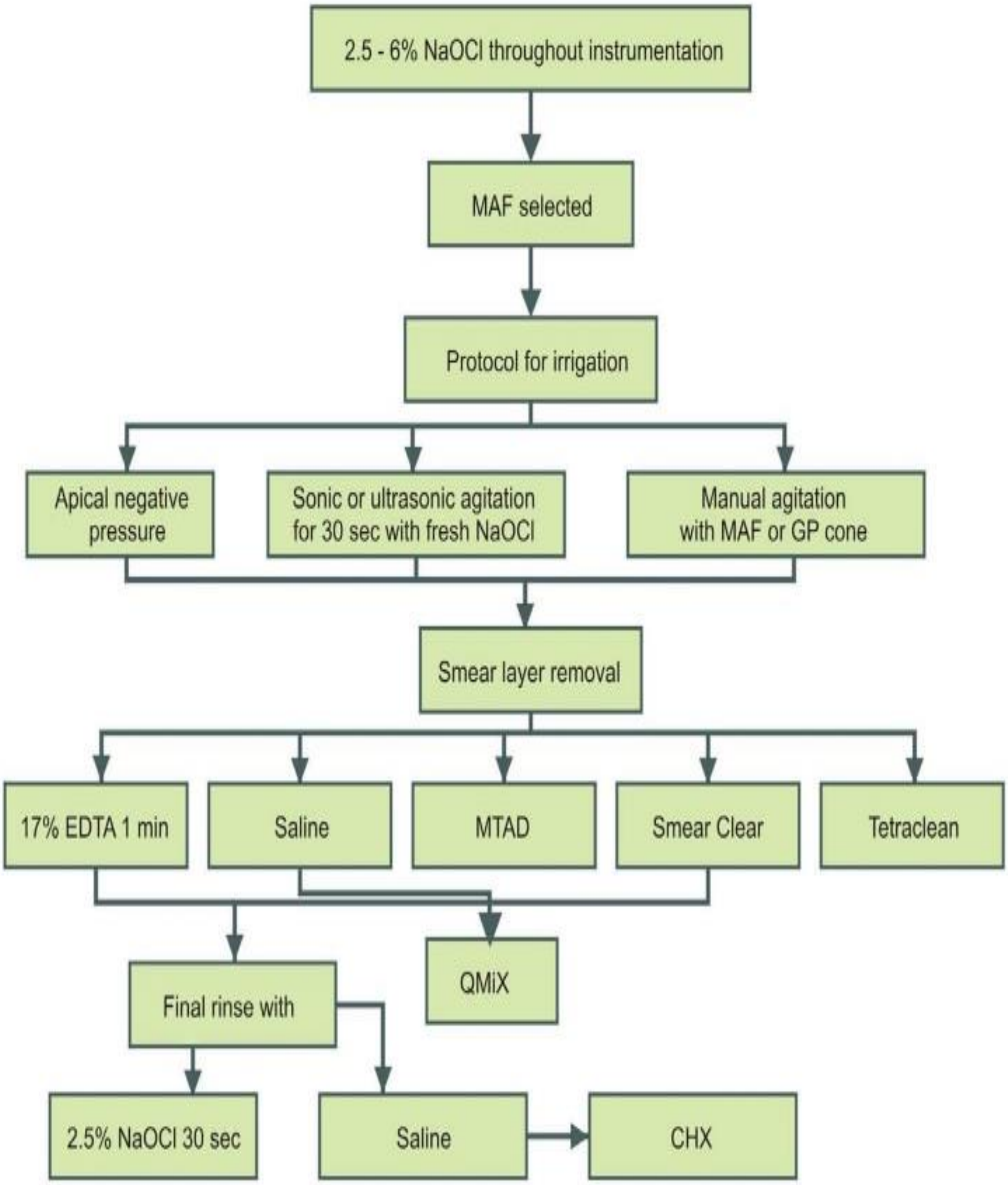


Figure 7: Recommended irrigation protocol for endodontics treatment (B. Basrani & Haapasalo, 2012)

Refrencess

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